U.S. National Phase Application

Filed January 26, 2005

Attorney Docket No.: 102286.155US1 Express Mail Label No. EV225199194US

Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

CLAIMS

1-21. (Canceled)

- 22. (New) A method of detecting a gene activation event in a cell *in vitro* or *in vivo*, the method comprising assaying a host cell stably transfected with a nucleic acid construct comprising a nucleic acid sequence encoding a member of the lipocalin protein family, or a transgenic non-human animal whose cells express such a construct, in which the cell or animal is subjected to a gene activation event that is signaled by expression of a peptide tagged lipocalin reporter gene.
- 23. (New) The method of claim 22, wherein the lipocalin protein is heterologous to the cell in which it is expressed.
- 24. (New) The method of claim 22, wherein the lipocalin protein is coded for by a nucleic acid construct comprising (i) a nucleic acid sequence encoding a member of the lipocalin protein family, and (ii) a nucleic acid sequence encoding a peptide sequence of from 5 to 250 amino acid residues.
- 25. (New) The method of claim 22, wherein the lipocalin is selected from the group consisting of: ovine betalactoglobulin (BLG) (accession No. X12817), murine major urinary protein (MUF) (accession No. NM 031188) and rat α -2-urinary globulin (α -2u) (accession number M27434).
- 26. (New) The method of claim 24, wherein the peptide sequence is an epitope.

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- 27. (New) The method of claim 26, wherein the epitope is selected from the group consisting of EQKLISEEDL, GKPIPNPLLGLDST, YPYDVPDYA, NVRFSTIVRRRA, KQMSDRRENDMSPS, SGNEVSRAVLLPQSC, SSLSYTNPAVAATSANL, RSTLQHPDYLQEYST, VSTLLRWERFPGHRQA, KFQQLVQCLTEFHAALGAYV, QEQCQEVWRKRVISAFLKSP, and RLSDKTGPVAQEKS.
- 28. (New) The method of claim 23, wherein the construct additionally comprises a promoter element upstream of the nucleic acid sequence comprising (i) a nucleic acid sequence encoding a member of the lipocalin protein family, and (ii) and nucleic acid sequence encoding a peptide sequence of from 5 to 250 amino acid residues.
- 29. (New) The method of claim 7, wherein the promoter element is selected from one of the groups consisting of:

c-myc, p21/WAF-1, MDM2, Gadd45, FasL, GAHSP40, TRAIL-R2/DR5, BTG2/PC3; MnSOD, CuZnSOD, IκB, ATF4, xanthine oxidase, COX2, iNOS, Ets-2, FasL/CD95L, γGCS, ORP150;

Lrg-21, SOCS-2, SOCS-3, PAI-1, GBP28/adiponectin, α-1 acid glycoprotein, metallothioneine I, metallothioneine II, ATF3, IGFbp-3, VDGF, HIF1α;

Gadd 34, GAHSP40, TRAIL-R2/DR5, c-fos, CHOP/Gaddl53, APAF-1, Gadd45, BTG2/PC3, Peg3/Pwl, Siahla, S29 ribosomal protein, FasL/CD95L, tissue tranglutaminase, GRP78, Nur77/NGFI-B, CyclophilinD, p73, Bak;

a promoter from a xenobiotic metabolizing cytochrome p450 enzyme from the 2A, 2B, 2C, 2D, 2E, 2S, 3A, 4A and 48 gene families; and

a synthetic promoter sequence comprised of a minimal eukaryote consensus promoter operatively linked to one or more response elements selected from the group consisting of the aryl hydrocarbon (Ah)/Ah nuclear translocator (ARNT) receptor response element, the antioxidant response element (ARE), the xenobiotic response element (XRE).

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30. (New) The method of claim 22, wherein the nucleic acid construct comprises a

stress inducible promoter operatively isolated from a nucleic acid sequence encoding a

member of the lipocalin protein family by a nucleotide sequence flanked by nucleic acid

sequences recognized by a site specific recombinase, or by insertion such that it is

inverted with respect to the transcription unit encoding a member of the lipocalin

protein family, in which the construct additionally comprises a nucleic acid sequence

comprising a tissue specific promoter operatively linked to a gene encoding the coding

sequence for the site specific recombinase.

31. (New) The method of claim 30, wherein the site-specific recombinase sequences

are two loxP sites of bacteriophage P1.

32. (New) The method of claim 22, wherein the gene activation event is induction of

toxicological stress, metabolic changes, or disease, including a disease that is the result

of viral, bacterial, fungal or parasitic infection.

33. (New) A method of screening for, or monitoring of toxicologically induced stress

in a cell or a cell line or a non-human animal, comprising the use of a cell, cell line or

non human animal which has been transfected with or carries a nucleic acid construct

as defined in claim 24.

34. (New) A method for screening and characterizing viral, bacterial, fungal, and

parasitic infection comprising the use of a cell, cell line or non human animal which has

been transfected with or carries a nucleic acid construct as defined in claim 24.

35. (New) A method for screening for cancer, inflammatory disease, cardiovascular

disease, metabolic disease, neurological disease and disease with a genetic basis

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comprising the use of a cell, cell line or non human animal which has been transfected with or carries a nucleic acid construct as defined in claim 24.